Constructing a fate map of the human embryo

Grant Award Details

Constructing a fate map of the human embryo

Grant Type: Comprehensive Grant

Grant Number: RC1-00113

Project Objective: Project objective is to generate a fate map of the early human embryo.

Investigator:

Name:	Susan Fisher
Institution:	University of California, San Francisco
Type:	PI

Human Stem Cell Use: Embryonic Stem Cell

Cell Line Generation: Embryonic Stem Cell

Award Value: $2,430,487

Status: Closed

Progress Reports

Reporting Period: Year 2

View Report

Reporting Period: Year 3

View Report

Reporting Period: Year 4

View Report

Reporting Period: Year 5 NCE

View Report

Grant Application Details

Application Title: Constructing a fate map of the human embryo

Public Abstract: The United States government does not fund research involving human embryos or cells that were grown from them after August 9, 2001. In addition, other restrictions have been imposed that make these types of experiments extremely difficult to do. For example, work cannot be conducted alongside research that is funded by government agencies, the typical mode in which academic research laboratories operate. In practical terms, this means that duplicate facilities must be created to do the large amount of research that is needed to turn human embryonic stem cells (hESCs) into robust experimental tools that will enable us to understand disease processes, the first step in curing them. These onerous regulations, unprecedented in our country, have stifled progress in this exciting new area of medical research. Thus, there is a great deal of basic work that remains to be accomplished. Our group is focusing on one particular area-the enigmatic process that occurs when an embryo-which would otherwise be discarded at the conclusion of an in vitro fertilization (IVF) treatment-is donated for research and grown in a laboratory. In certain cases, the cells that would have gone on to form specialized tissues such as blood cells, and major organs such as the heart and pancreas, continue to make copies of themselves. As first shown in 1998, the copies, termed hESC lines, may remember how to do their original job, i.e., differentiate into every type of cell in the human body. Scientists think that this is possible, because in many laboratory animals the equivalent populations retain this ability. Our group wants to optimize the methods that are used to make new hESC lines, because the techniques that are currently used are essentially random. Embryos are maintained in the laboratory until outgrowths-collections of cells that look very different from one another-appear. During this 2 to 3-week process, many of these cells die, but a subset start to make copies of themselves. Thus, much remains to be learned about the derivation process. For example, we do not know when, during this extended time period, the actual progenitor cell(s) arises, and it is unclear whether all the cells of the embryo are equally able to give rise to hESC lines. Thus, we propose to test the theory that there are better, more controlled ways to produce hESCs. Recently, our collaborators showed that it is possible to make lines from single cells that are removed from human embryos at a specific time. We want to use their method to determine if hESCs made from individual cells that are removed at different times from specific regions of the embryo are better equipped to generate all the cell types found in the body. Essentially, we want to harness and standardize the process of developing new lines. This work, which cannot be supported by the federal government, has important implications for devising hESC-based patient therapies.
Statement of Benefit to California (prov

Statement of Benefit to California:	The people of California have gained in substantive ways from the biotechnology revolution, which was fueled by research done in the Bay Area beginning in the mid-1970s. The benefits to the state's citizens that were provided by this sea change in the practice of science were summarized at the BIO meeting that was held in San Francisco in 2004. The economic rewards are clear. In 2000, it was estimated that nearly a quarter of a million Californians, including 50,000 biological scientists-11.5% of the nation's total workforce-were employed by the biotechnology sector. These individuals worked for 2,500 biomedical companies and in the state's public and private research institutions. Recent estimates suggest that, during this same time period, the biotechnology industry generated $7.8 billion in worldwide revenue and $6.4 billion in exports. The intellectual benefits are numerous, as talented scientists at all stages of their careers have joined California's biotechnology community to be part of an exciting new industry that translates basic research into new patient therapies. The medical benefits are also clear, as these companies are targeting unmet medical needs in numerous areas, such as cardiovascular, autoimmune and respiratory diseases, cancer, and HIV/AIDS and other infectious diseases. Also during this time period, California's research institutions received more National Institutes of Health (NIH) grant funding than any other state, totaling $2.3 billion in 2000. Thus, for the last 40 years, synergy between California's private and public research enterprises has produced major medical advances that have improved the lives of millions of people here and around the world. Now we are on the brink of another scientific revolution that was sparked by the first report of methods for the isolation and propagation of human embryonic stem cells (hESC), which was published by Dr. James Thomson in 1998. However, in an unprecedented move, the United States government decided in 2001 to restrict work in this burgeoning new area by limiting research to hESC lines that were submitted to the Federal Registry by August 9 of that year. It is clear that only a small fraction of the lines that were registered are actually hESCs. Consequently, NIH-funded research is limited to cell lines that have been in culture for many years and that were generated using suboptimal methods. Thus, the field is at an impasse. To go forward, we need NIH-level funds to do the basic work that is needed to develop this exciting field, which many scientists envision will fuel research in the public and private sectors for decades to come. With the passage of Proposition 71 in 2004 and the creation of the Institute for Regenerative Medicine, California has stepped into the breach. As a result, the state will once again reap the economic, intellectual and medical benefits that an exciting new area of research creates.

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